REMARKS

Claims 3-7 and 15-22 are pending in this application. Claims 1-2 and 8-14 have been canceled. Claim 17 has been amended as discussed below.

Applicant gratefully acknowledges the Examiner's statement that claims 3, 4 and 22 are allowable.

Prior Art Rejections

35 U.S.C. §102(b)

Claims 1 and 2 were rejected under 35 U.S.C. §102(b) as being anticipated by Brana et al. Claims 1 and 2 have been canceled thus obviating the rejection.

35 U.S.C. §102(e)

Claims 5-11 and 14-21 were rejected under 35 U.S.C. §102(e) as being anticipated by Ajami et al. Claims 8-14 have been canceled. Applicant respectfully traverse the rejection as it applies to pending claims 5-7 and 15-21.

Claims 5-7

The Applicant conceived of and reduced to practice the method of claim 5 prior to the earliest priority date available to the Ajami et al patent. Applicant submits a declaration under 37 CFR §1.131 by inventor Dennis M. Brown setting forth the details of the invention and reduction to practice of the invention as claimed. As shown in Exhibit A, the Applicant used the claimed method to generate a diammonium salt of a naphthalimide. Specifically, the Applicant generated amonafide dihydrochloride using the method disclosed in the specification and presently claimed.

Based on the above presented facts, Applicant submits that the invention as claimed was invented and reduced to practice by the Applicant prior to April 22, 2002, the earliest priority date of the Ajami et al patent. Accordingly, Applicant requests removal of this rejection as it applies to claim 5 and claims 6-7 dependent thereon.

Claims 15-21

For anticipation under 35 U.S.C. 102, the reference must teach every element of the claimed invention. MPEP 706.02. With regards to the rejection of claims 15-21, Applicant asserts that Ajami et al. does not teach the aqueous solutions of these claims.

Claim 15 recites an aqueous solution consisting essentially of a dissolved amonafide diammonium salt in a solution suitable for administration by injection, where the solution comprises amonafide at between 1 and 250 mg/mL and having a pH between 4.0 and 7.0. Ajami et al. does not disclose such a solution. Ajami generally discloses general administration procedures (see column 8) but does not discloses solutions comprising amonafide at between 1 and 250 mg/mL having a pH between 4.0 and 7.0.

Claim 17 recites an aqueous solution of amonafide diammonium salt in a solution suitable for administration by injection, where the solution comprises amonafide at between 10 and 100 mg/mL having a pH between 5.5 and 6.5. Dependent claims 18-21 respectively provide the additional elements that the solution is substantially free of sugars, that the solution further comprises a pharmaceutically acceptable carrier, that the carrier is provided at a concentration between about 0.1 to 100 mg/mL, and that the solution is provided in a unit dosage form. Ajami et al. does not teach the solution as disclosed in claims 17-21. As discussed above, Ajami et al. generally discloses general administration procedures but does disclose the all of the claim elements of claims 17-21.

Because Ajami et al. does not discloses each and every element of claims 15-21 it does not anticipate the claims. Applicant requests withdrawal of this rejection.

35 U.S.C. §103(a)

Claims 5-21 were rejected under 35 U.S.C. §103(a) as being obvious over Brana et al and Brana et al I (US 5,420,137) in view of Brana II (US 5,552,544). Claims 8-14 have been canceled. Applicant respectfully traverse the rejection as it applies to pending claims 5-7 and 15-21. Applicant notes that Claim 17 has been amended to recite the limitation of a diammonium salt.

In order to establish a *prima facie* case of obviousness, the Examiner must show that the cited prior art references teach or suggest all the claim limitations and that there is motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings to arrive at the present invention. Applicant asserts that the Examiner has failed to present a *prima facie* case of obviousness.

The Examiner has cited Brana et al. for teaching an acetyl ammonium salt of naphthalimide and Brana I for teaching monohydrochloride and monomethanesulfonate salts of amonafide. As acknowledged by the Examiner, neither of these references teaches a diammonium salt of naphthalimide having two counter ions attached to the two nitrogens. The Examiner relies on Brana II to supply the missing teaching of a diammonium salt of a naphthalimide. Applicant respectfully disagrees. Brana II provides a list of possible acids that may be used to form salts of a specifically disclosed naphthalimide. Brana II then teaches that the naphthalmides can be converted to their salts in a "conventional manner, for example by reacting with an acid." However, as indicted by the teachings of Brana I, the "conventional manner" was to generate only the monoammonium salt of naphthalimide using a set amount of acid. As such, the combination of references relied on by the Examiner fails to teach all of the limitations of the invention as presently claimed.

The Examiner further contends that it would be obvious to one of skill in the art to modify the teachings of the cited references to form a monoammonium salt of naphthalimide first and then add excess acid to form the diammonium salt. However, the Examiner has not provided any support for this contention. Rather, it appears that the Examiner is relying on the

teachings of the instant specification to provide the motivation to add the excess acid to arrive at the present invention. Such reliance is impermissible. The Federal Circuit has cautioned against "fall[ing] victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *See, e.g., In re Dembiczak,* 50 USPQ2d 1614, 1617 (Fed. Cir. 1999).

Additionally, with respect to claims 15 and 16, none of the cited references teach or suggest aqueous solutions consisting essentially of a dissolved amonafide diammonium, where the solution is suitable for administration by injection, where the solution comprises amonafide at between 1 and 250 mg/mL having a pH between 4.0 and 7.0.

Similarly, none of the recited references teach or suggest the solutions recited in claims 17-21. Claim 17 recites an aqueous solution of amonafide diammonium salt in a solution suitable for administration by injection, where the solution comprises amonafide at between 10 and 100 mg/mL having a pH between 5.5 and 6.5. Dependent claims 18-21 respectively provide the additional elements that the solution is substantially free of sugars, that the solution further comprises a pharmaceutically acceptable carrier, that the carrier is provided at a concentration between about 0.1 to 100 mg/mL, and that the solution is provided in a unit dosage form.

Brana et al. makes no mention of aqueous amonafide solutions. Brana I discloses making an injectable solution of a monoammonium salt of amonafide but does not disclose diammonium salts or solutions containing those salts. Brana II only mentions solutions of the compounds disclosed therein in a very general sense. None of the references teach or fairly suggest the limitations set forth in claims 15-21 of the present invention.

For the reasons set forth above, Applicant asserts that claims 5-7 and 15-21 are non-obvious over the cited references and requests withdrawal of the rejection.

CONCLUSION

Applicant respectfully requests that the present remarks be considered and submits that the claims are in condition for allowance. An early notification of such is requested. The Examiner is invited to call the undersigned attorney for discussion of any outstanding issues.

Respectfully submitted,

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